General

Guideline Title

Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus.

Bibliographic Source(s)

National Academy of Clinical Biochemistry (NACB). Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. Washington (DC): National Academy of Clinical Biochemistry (NACB); 2011. 104 p. [378 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Sacks DB, Bruns DE, Goldstein DE, Maclaren NK, McDonald JM, Parrott M. Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. Clin Chem 2002 Mar;48(3):436-72.

The next review of this guideline is planned in 5 years, unless substantial new evidence emerges earlier for high-priority areas in the laboratory management of patients with diabetes mellitus.

Recommendations

Major Recommendations

Definitions of the quality of evidence (high, moderate, low, and very low) and the strength of recommendations (A, B, C, Good Practice Points [GPPs]) are presented at the end of the "Major Recommendations" field.

Glucose

Use

Diagnosis/Screening

Recommendation: When glucose is used to establish the diagnosis of diabetes, it should be measured in venous plasma. A (high)

Recommendation: When glucose is used for screening of high-risk individuals, it should be measured in venous plasma. B (moderate)

Recommendation: Plasma glucose should be measured in an accredited laboratory when used for diagnosis of or screening for diabetes. Good Practice Point (GPP)

Recommendation: Outcome studies are needed to determine the effectiveness of screening. C (moderate)

Monitoring/Prognosis

Recommendation: Routine measurement of plasma glucose concentrations in an accredited laboratory is not recommended as the primary means of monitoring or evaluating therapy in individuals with diabetes. B (low)

Analytical Considerations

Preanalytical

Recommendation: To minimize glycolysis, one should place the sample tube immediately in an ice-water slurry, and the plasma should be separated from the cells within 30 min. If that cannot be achieved, a tube containing a rapidly effective glycolysis inhibitor, such as citrate buffer, should be used for collecting the sample. Tubes with only enolase inhibitors, such as sodium fluoride, should not be relied on to prevent glycolysis. B (moderate)

Recommendation: Blood for fasting plasma glucose (FPG) analysis should be drawn in the morning after the individual has fasted overnight (at least 8 hours). B (low)

Analytical

Recommendation: On the basis of biological variation, glucose measurement should have an analytical imprecision ≤2.9%, a bias ≤2.2%, and a total error ≤6.9%. To avoid misclassification of patients, the goal for glucose analysis should be to minimize total analytical error, and methods should be without measurable bias. B (low)

Glucose Meters

Use

Diagnosis/Screening

Recommendation: There are insufficient published outcome data to support a role for portable meters and skin-prick (finger-stick) blood samples in the diagnosis of diabetes or for population screening. C (moderate)

Recommendation: The imprecision of the results, coupled with the substantial differences among meters, precludes the use of glucose meters from the diagnosis of diabetes and limits their usefulness in screening for diabetes. A (moderate)

Monitoring/Prognosis

Recommendation: Self-monitoring of blood glucose (SMBG) is recommended for all insulin-treated patients with diabetes. A (high)

Recommendation: In patients with type 2 diabetes treated with diet and oral agents, SMBG may help achieve better control, particularly when therapy is initiated or changed. Data are insufficient, however, to claim an associated improvement of health outcomes. The role of SMBG in patients with stable type 2 diabetes controlled by diet alone is not known. C (high)

Analytical Considerations

Preanalytical

Recommendation: Patients should be instructed in the correct use of glucose meters, including quality control. Comparison between SMBG and concurrent laboratory glucose analysis should be performed at regular intervals to evaluate the performance of the meters in the patient's hands. B (moderate)

Analytical

Recommendation: Multiple performance goals for portable glucose meters have been proposed. These targets vary widely and are highly controversial. Manufacturers should work to improve the imprecision of current meters, with an intermediate goal of limiting total error for 95% of samples to ≤15% at glucose concentrations ≥5.6 mmol/L (100 mg/dL) and to <0.8 mmol/L (15 mg/dL) at glucose concentrations <5.6 mmol/L (100 mg/dL). Lower total error would be desirable and may prove necessary in tight glucose-control protocols and for avoiding hypoglycemia in all settings. C (low)

Recommendation: Meters should measure and report plasma glucose concentrations to facilitate comparison with assays performed in accredited laboratories. GPP

Recommendation: Studies are needed to determine the analytical goals (quality specifications) for glucose meters in SMBG and in intensive care units (ICUs). C (moderate)

Recommendation: For future research: important end points in studies of SMBG should include, at a minimum, hemoglobin A1c (HbA_{1c}) and frequency of hypoglycemic episodes to ascertain whether improved meters enable patients to achieve better glucose control. For studies of meter use in intensive or critical care, important end points include mean blood glucose, frequency of hypoglycemia, and variation of glucose control. Ideally, outcomes (e.g., long-term complications) should also be examined. GPP

Continuous Minimally Invasive Glucose Analyses

Use

Recommendation: Real-time continuous glucose monitoring (CGM) in conjunction with intensive insulin regimens can be a useful tool to lower HbA_{1c} in selected adults (age >25 years) with type 1 diabetes. A (high)

Recommendation: Although the evidence for lowering HbA_{1c} is not as strong for children, teens, and younger adults, real-time CGM may be helpful in these groups. Success correlates with adherence to ongoing use of the device. B (moderate)

Recommendation: Real-time CGM may be a supplemental tool to SMBG in individuals with hypoglycemia unawareness and/or frequent episodes of hypoglycemia. B (low)

Recommendation: Patients require extensive training in using the device. Available devices must be calibrated with SMBG readings, and the latter are recommended for making treatment changes. GPP

Noninvasive Glucose Analysis

Use

Recommendation: No noninvasive sensing technology is currently approved for clinical glucose measurements of any kind. Major technological hurdles must be overcome before noninvasive sensing technology will be sufficiently reliable to replace existing portable meters, implantable biosensors, or minimally invasive technologies. C (very low)

Gestational Diabetes Mellitus (GDM)

Use

Recommendation: All pregnant women not previously known to have diabetes should undergo testing for GDM at 24 to 28 weeks of gestation. A (high)

Interpretation

Recommendation: GDM should be diagnosed by a 75-g oral glucose tolerance test (OGTT) according to the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria derived from the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study. A (moderate)

Urinary Glucose

Use

Recommendation: Semiquantitative urine glucose testing is not recommended for routine care of patients with diabetes mellitus. B (low)

Ketone Testing

Use

Recommendation: Ketones measured in urine or blood in the home setting by patients with diabetes and in the clinic/hospital setting should be considered only an adjunct to the diagnosis of diabetic ketoacidosis (DKA). GPP

Interpretation

Recommendation: Urine ketone measurements should not be used to diagnose or monitor the course of DKA. GPP

Recommendation: Blood ketone determinations that rely on the nitroprusside reaction should be used only as an adjunct to diagnose DKA and

should not be used to monitor DKA treatment. Specific measurement of beta-hydroxybutyric acid (βHBA) in blood can be used for diagnosis and monitoring of DKA. B (moderate)

HbA_{1c}

Use

Recommendation: HbA_{1c} should be measured routinely in all patients with diabetes mellitus to document their degree of glycemic control. A (moderate)

Analytical Considerations

Recommendation: Laboratories should use only HbA_{1c} assay methods that are certified by the National Glycohemoglobin Standardization Program (NGSP) as traceable to the Diabetes Control and Complications Trial (DCCT) reference. The manufacturers of HbA_{1c} assays should also show traceability to the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) reference method. GPP

Recommendation: Laboratories that measure HbA_{1c} should participate in a proficiency-testing program, such as the College of American Pathologists (CAP) HbA_{1c} survey, that uses fresh blood samples with targets set by the NGSP Laboratory Network. GPP

Preanalytical

Recommendation: Laboratories should be aware of potential interferences, including hemoglobinopathies, that may affect HbA_{1c} test results, depending on the method used. In selecting assay methods, laboratories should consider the potential for interferences in their particular patient population. In addition, disorders that affect erythrocyte turnover may cause spurious results, regardless of the method used. GPP

Analytical

Recommendation: Samples with HbA_{1c} results below the lower limit of the reference interval or >15% HbA_{1c} should be verified by repeat testing. B (low)

Recommendation: HbA_{1c} values that are inconsistent with the clinical presentation should be investigated further. GPP

Interpretation

Clinical Application

Recommendation: Treatment goals should be based on American Diabetic Association (ADA) recommendations, which include generally maintaining HbA_{1c} concentrations at <7% and more-stringent goals in selected individual patients if they can be achieved without significant hypoglycemia or other adverse treatment effects. Somewhat higher intervals are recommended for children and adolescents and may be appropriate for patients with a limited life expectancy, extensive comorbid illnesses, a history of severe hypoglycemia, or advanced complications (note that these values are applicable only if the NGSP has certified the assay method as traceable to the DCCT reference). A (high)

Recommendation: HbA_{1c} testing should be performed at least biannually in all patients and quarterly for patients whose therapy has changed or who are not meeting treatment goals. B (low)

Emerging Considerations

Recommendation: HbA_{1c} may be used for the diagnosis of diabetes, with values >6.5% being diagnostic. An NGSP-certified method should be performed in an accredited laboratory. Analogous to its use in the management of diabetes, factors that interfere with or adversely affect the HbA_{1c} assay will preclude its use in diagnosis. A (moderate)

Recommendation: Point-of-care HbA_{1c} assays are not sufficiently accurate to use for the diagnosis of diabetes. B (moderate)

Genetic Markers

Use

Diagnosis/Screening

Recommendation: Routine measurement of genetic markers is not of value at this time for the diagnosis or management of patients with type 1 diabetes. For selected diabetic syndromes, including neonatal diabetes, valuable information can be obtained with definition of diabetes-associated mutations. A (moderate)

Recommendation: There is no role for routine genetic testing in patients with type 2 diabetes. These studies should be confined to the research setting and evaluation of specific syndromes. A (moderate)

Autoimmune Markers

Use

Recommendation: Islet cell autoantibodies are recommended for screening nondiabetic family members who wish to donate part of their pancreas for transplantation to a relative with end-stage type 1 diabetes. B (low)

Recommendation: Islet cell autoantibodies are not recommended for routine diagnosis of diabetes, but standardized islet cell autoantibody tests may be used for classification of diabetes in adults and in prospective studies of children at genetic risk for type 1 diabetes after human leukocyte antigen (HLA) typing at birth. B (low)

Diagnosis/Screening

Recommendation: Screening patients with type 2 diabetes for islet cell autoantibodies is not recommended at present. Standardized islet cell autoantibodies are tested in prospective clinical studies of type 2 diabetes patients to identify possible mechanisms of secondary failures of treatment of type 2 diabetes. B (low)

Recommendation: Screening for islet cell autoantibodies in relatives of patients with type 1 diabetes or in persons from the general population is not recommended at present. Standardized islet cell autoantibodies are tested in prospective clinical studies. B (low)

Monitoring/Prognosis

Recommendation: There is currently no role for measurement of islet cell autoantibodies in the monitoring of patients in clinical practice. Islet cell autoantibodies are measured in research protocols and some clinical trials as surrogate end points. B (low)

Analytical Considerations

Recommendation: It is important that autoantibodies be measured only in an accredited laboratory with an established quality-control program and participation in a proficiency-testing program. GPP

Albuminuria (formerly Microalbuminuria)

Use

Recommendation: Annual testing for albuminuria in patients without clinical proteinuria should begin in pubertal or postpubertal individuals 5 years after diagnosis of type 1 diabetes and at the time of diagnosis of type 2 diabetes, regardless of treatment. B (moderate)

Recommendation: Urine albumin at concentrations ≥30 mg/g creatinine should be considered a continuous risk marker for cardiovascular events. B (moderate)

Analytical Considerations

Recommendation: The analytical coefficient of variation (CV) of methods to measure low levels of albuminuria should be <15%. B (moderate)

Analytical

Recommendation: Semiquantitative or qualitative screening tests should be positive in >95% of patients with low levels of albuminuria to be useful for screening. Positive results must be confirmed by analysis in an accredited laboratory. GPP

Recommendation: Currently available dipstick tests do not have adequate analytical sensitivity to detect low levels of albuminuria. B (moderate)

Recommendation: Acceptable samples to test for increased urinary albumin excretion are timed collections (e.g., 12 or 24 hours) for measurement of the albumin concentration and timed or untimed samples for measurement of the albumin–creatinine ratio. B (moderate)

Recommendation: The optimal time for spot urine collection is the early morning. All collections should be at the same time of day to minimize variation. The patient should not have ingested food within the preceding 2 hours but should be well hydrated (i.e., not volume depleted). GPP

Interpretation

Recommendation: Low urine albumin concentrations (i.e., <30 mg/g creatinine) are not associated with high cardiovascular risk if the estimated glomerular filtration rate (eGFR) is >60 mL · min^{-1} · $(1.73\ m^2)^{-1}$ and the patient is normotensive. If the eGFR is <60 mL · min^{-1} · $(1.73\ m^2)^{-1}$ and/or the level of albuminuria is >30 mg/g creatinine on a spot urine sample, a repeat measurement should be taken within the year to assess change among people with hypertension. A (moderate)

Miscellaneous Potentially Important Analytes. I. Insulin and Precursors

Use

Recommendation: There is no role for routine testing for insulin, C-peptide, or proinsulin in most patients with diabetes. Differentiation between type 1 and type 2 diabetes may be made in most cases on the basis of the clinical presentation and subsequent course. These assays are useful primarily for research purposes. Occasionally, C-peptide measurements may help distinguish type 1 from type 2 diabetes in ambiguous cases, such as patients who have a type 2 phenotype but present in ketoacidosis. B (moderate)

Recommendation

There is no role for measurement of insulin concentration in the assessment of cardiometabolic risk, because knowledge of this value does not alter the management of these patients. B (moderate)

Analytical Considerations

Recommendation: Because current measures of insulin are poorly harmonized, a standardized insulin assay should be developed to encourage the development of measures of insulin sensitivity that will be practical for clinical care. GPP

Miscellaneous Potentially Important Analytes. II. Insulin Antibodies

Recommendation: There is no published evidence to support the use of insulin antibody testing for routine care of patients with diabetes. C (very low)

Definitions:

The Overall Quality of the Body of Evidence

High: Further research is very unlikely to change the confidence in the estimate of effect. The body of evidence comes from high-level individual studies that are sufficiently powered and provide precise, consistent, and directly applicable results in a relevant population.

Moderate: Further research is likely to have an important impact on the confidence in the estimate of effect and may change the estimate and the recommendation. The body of evidence comes from high-/moderate-level individual studies that are sufficient to determine effects, but the strength of the evidence is limited by the number, quality, or consistency of the included studies; by the generalizability of results to routine practice; or indirect nature of the evidence.

Low: Further research is very likely to have an important impact on the confidence in the estimate of effect and is likely to change the estimate and the recommendation. The body of evidence is of low level and comes from studies with serious design flaws or with evidence that is indirect.

Very low: Any estimate of effect is very uncertain. Recommendation may change when higher-quality evidence becomes available. Evidence is insufficient to assess the effects on health outcomes because of limited number or power of studies, important flaws in their design or conduct, gaps in the chain of evidence, or lack of information.

The Strength of Recommendations

A. The National Academy of Clinical Biochemistry (NACB) Strongly Recommends Adoption.

Strong recommendations *for* adoption are made when:

- There is high-quality evidence and strong or very strong agreement of experts that the intervention improves important health outcomes and that benefits substantially outweigh harms; *or*
- There is moderate-quality evidence and strong or very strong agreement of experts that the intervention improves important health outcomes and that benefits substantially outweigh harms.

Strong recommendations *against* adoption are made when:

- There is high-quality evidence and strong or very strong agreement of experts that the intervention is ineffective or that benefits are closely balanced with harms, or that harms clearly outweigh benefits; *or*
- There is moderate-quality evidence and strong or very strong agreement of experts that the intervention is ineffective or that benefits are closely balanced with harms, or that harms outweigh benefits.

B. The NACB Recommends Adoption.

Recommendations *for* adoption are made when:

- There is moderate-quality evidence and level of agreement of experts that the intervention improves important health outcomes and that benefits outweigh harms; *or*
- There is low-quality evidence but strong or very strong agreement and high level of confidence of experts that the intervention improves important health outcomes and that benefits outweigh harms; *or*
- There is very low-quality evidence but very strong agreement and very high level of confidence of experts that the intervention improves important health outcomes and that benefits outweigh harms.

Recommendations *against* adoption are made when:

- There is moderate-quality evidence and level of agreement of experts that the intervention is ineffective or that benefits are closely balanced with harms, or that harms outweigh benefits; *or*
- There is low-quality evidence but strong or very strong agreement and high level of confidence of experts that the intervention is ineffective or that benefits are closely balanced with harms, or that harms outweigh benefits; *or*
- There is very low-quality evidence but very strong agreement and very high level of confidence of experts that the intervention is ineffective or that benefits are closely balanced with harms, or that harms outweigh benefits.

C. The NACB Concludes That There Is Insufficient Information to Make a Recommendation.

Grade C is applied in the following circumstances:

- Evidence is lacking, scarce, or of very low quality, the balance of benefits and harms cannot be determined, and there is no or very low level of agreement of experts for or against adoption of the recommendation.
- At any level of evidence—particularly if the evidence is heterogeneous or inconsistent, indirect, or inconclusive—if there is no agreement of experts for or against adoption of the recommendation.

Good Practice Point (GPP). The NACB Recommends It as Good Practice Point.

GPPs are recommendations mostly driven by expert consensus and professional agreement and are based on the information listed below and/or professional experience, or widely accepted standards of best practice. This category applies predominantly to technical (e.g., preanalytical, analytical, postanalytical), organizational, economic, or quality-management aspects of laboratory practice. In these cases, evidence often comes from observational studies, audit reports, case series or case studies, nonsystematic reviews, guidance or technical documents, non–evidence-based guidelines, personal opinions, expert consensus, or position statements. Recommendations are often based on empirical data, usual practice, quality requirements, and standards set by professional or legislative authorities or accreditation bodies, etc.

Clinical Algorithm(s)

An algorithm for urine protein testing is provided in the original guideline document.

Scope

Disease/Condition(s)

Type 1 and type 2 diabetes mellitus

Note: This guideline is primarily focused on the laboratory aspects of testing in the contexts of type 1 and type 2 diabetes mellitus (DM). This guideline does not deal with any issues related to the clinical management of diabetes mellitus (DM) that are already covered in the American Diabetes Association (ADA) or World Health Organization (WHO) guidelines.

Guideline Category

Diagnosis

Management

Screening

Clinical Specialty

Endocrinology

Family Practice

Internal Medicine

Pathology

Intended Users

Clinical Laboratory Personnel

Health Care Providers

Nurses

Patients

Physician Assistants

Physicians

Guideline Objective(s)

- To supplement the American Diabetes Association (ADA) recommendations on diagnosis and management of diabetes mellitus (DM)
- To focus on practical aspects of care to assist in making decisions related to the use or interpretation of laboratory tests during screening, diagnosing, or monitoring of patients with DM

Target Population

Patients with diabetes mellitus

Interventions and Practices Considered

Diagnosis/Screening

1. Measurement of glucose in venous plasma
2. Measurement of plasma glucose in an accredited laboratory
3. Testing of all pregnant women not previously known to have diabetes for gestational diabetes mellitus (GDM) at 24–28 weeks of gestation using oral glucose tolerance test (OGTT)
4. Ketone measurement as an adjunct to diagnosis of diabetic ketoacidosis
5. HbA_{1c} as an emerging marker for diabetes screening and diagnosis

Management/Monitoring

1. Use of self-monitoring of blood glucose (SMBG) for all insulin-treated patients with diabetes

2. Instruction of patients in correct use of glucose meters
3. Use of a real-time continuous glucose monitoring (CGM) device
4. Training patients in use of CGM devices
5. Routine HbA_{1c} testing in all patients with diabetes mellitus
6. Annual testing for albuminuria in patients without clinical proteinuria

Note: The following were considered but not recommended: portable meters and skin-prick blood tests for screening or diagnosis; noninvasive glucose analyses; urine glucose testing; routine testing of genetic markers; islet cell autoantibodies for routine diagnosis, screening, or management of diabetes; routine testing for insulin, C-peptide, or proinsulin.

Major Outcomes Considered

- Misclassification and mismanagement of patients
- Cardiovascular disease
- Frequency of large babies (macrosomia)
- Long-term complications of disease
- Efficacy of screening

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

Key questions that earned the highest priority score (see Step 4 in the original guideline document) were covered by a more systematic approach during the search and evaluation of the evidence currently available in the literature. Other topics that were considered less important were dealt with in a less rigorous way. Because this guideline is an update of the 2002 version, authors limited their searches to the period beginning in January 2002. Guidelines related to the topic were searched in the Agency for Healthcare Research and Quality National Guideline Clearinghouse database. Systematic reviews and meta-analyses were searched by using the Clinical Queries–Find Systematic Reviews function of PubMed. If no such publications were found, PubMed, EMBASE, and other databases were used to search the primary literature. Because the group of authors included leading experts in their fields, the authors' personal files, communications with experts, and unpublished or ongoing-trial data were also made available to be used in the guideline-updating process. Additional literature citations were added during the comment periods.

Authors selected relevant key publications for updating each section, and the editor of the guideline and lead authors of other sections acted as independent expert reviewers to avoid biased selection of papers. When the guideline team retrieved and agreed with existing guideline recommendations that had already covered the key question comprehensively and had reached concordant conclusions, the guideline team simply adopted and referenced the published recommendations in order to avoid duplicate publication.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

The Overall Quality of the Body of Evidence

High: Further research is very unlikely to change the confidence in the estimate of effect. The body of evidence comes from high-level individual studies that are sufficiently powered and provide precise, consistent, and directly applicable results in a relevant population.

Moderate: Further research is likely to have an important impact on the confidence in the estimate of effect and may change the estimate and the recommendation. The body of evidence comes from high-/moderate-level individual studies that are sufficient to determine effects, but the strength of the evidence is limited by the number, quality, or consistency of the included studies; by the generalizability of results to routine practice; or indirect nature of the evidence.

Low: Further research is very likely to have an important impact on the confidence in the estimate of effect and is likely to change the estimate and the recommendation. The body of evidence is of low level and comes from studies with serious design flaws or with evidence that is indirect.

Very low: Any estimate of effect is very uncertain. Recommendation may change when higher-quality evidence becomes available. Evidence is insufficient to assess the effects on health outcomes because of limited number or power of studies, important flaws in their design or conduct, gaps in the chain of evidence, or lack of information.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Critical review of selected key publications formed the basis for establishing the level and quality of the evidence underlying each recommendation (see the "Rating Scheme for the Strength of the Evidence" field). Section authors and a methodology expert extracted data into evidence tables (see Table 3 in the Appendix to the original guideline). These tables list all key questions together with their priority scores. Related recommendations and their grades from the 2002 guideline were aligned with those of the new updated recommendations (see columns 1 and 2 in Appendix Table 3). In the updated recommendation, authors highlighted changes to the original text in boldface and provided explanation for the changes where necessary (column 3). Key references supporting the new recommendation were listed (column 4).

To the authors' knowledge, no uniformly accepted grading scheme exists for rating the quality of evidence and the strength of recommendations when questions related to laboratory testing for the screening, diagnosis, prognosis, and monitoring of a condition are addressed. The guideline group agreed that the grading scheme of the American Diabetic Association (ADA), which was used in the 2002 version of this guideline, is applicable predominantly to therapeutic recommendations and that its use in this diagnostic guideline was thus impracticable. Therefore, the guideline group developed a grading system by adapting the key elements of evidence-rating frameworks employed by various international guideline agencies, the US Preventive Services Task Force, and the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group. In this system, the overall quality of the body of evidence (see the "Rating Scheme for the Strength of the Evidence" field) and the strength of recommendations (see the "Rating Scheme for the Strength of the Recommendations" field) are graded separately. Rating the quality of the body of evidence is based on (a) the level of evidence of *individual* studies defined by their study design and methodological quality; (b) the consistency of results across various studies; (c) the directness of comparisons; and (d) the precision-of-effect estimates. Table 1 in the original guideline document provides a detailed explanation of evidence-level categories and these elements of the rating scheme for the quality of evidence.

Members of the guideline committee received detailed explanations and guidance, as well as methodological support, on how to use the grading scheme. At this stage of the guideline-development process, section authors indicated the study design (see column 5 in Table 3 of the Appendix to the original guideline) and the level of evidence (column 6) of all individual studies listed in the evidence tables. The quality of the totality of the evidence underlying each recommendation was established by means of the criteria mentioned above (column 7).

Methods Used to Formulate the Recommendations

Expert Consensus (Consensus Development Conference)

Description of Methods Used to Formulate the Recommendations

The guideline committee included representatives of key stakeholders to whom the recommendations are meant to apply primarily. The guideline committee included clinical experts and laboratory experts whose key area of research and practice is diabetes mellitus (DM). Some members of the committee provided additional support in evidence-based guideline-development methodology.

The chairman of the guideline committee acted as editor and assigned lead authors to each section. Authors reviewed the 2002 edition of the National Academy of Clinical Biochemistry (NACB) DM guideline and identified key areas for revisions and updating. The guideline team discussed the scope and methods of the updating process at a face-to-face meeting, which was followed by numerous teleconferences and e-mail exchanges among authors that were coordinated by the editor and the NACB. The guideline group decided that the structure of the guideline would remain the same as the 2002 document and that it would cover virtually all key analytes that are used primarily in the diagnosis and management of individuals with DM. As before, the testing of lipids and related cardiovascular risk factors is not covered in this update but is addressed in a separate NACB guideline.

The first draft of the guideline was released on the National Academy of Clinical Biochemistry (NACB) Web site for soliciting of public review and feedback. The still non-graded draft recommendations were sent to a number of external organizations (see Table 1 in the Appendix to the original guideline document) for peer review and expert comments that could be submitted either via the NACB Web site or by mail. The draft guideline was also presented at the Arnold O. Beckman consensus conference in 2007, and the discussions at this conference were recorded.

The guideline team reviewed and discussed the comments that were received and made many changes to the first draft to reflect the views of external peers, organizations, or individuals. The amended draft of the guideline was also presented at the 2009 American Association for Clinical Chemistry (AACC) annual meeting and used for grading recommendations.

Recommendations in diagnostic guidelines frequently are supported primarily by expert consensus. This reflects the often poor quality of evidence, or the lack or indirectness of evidence that the intervention is relevant to patient outcomes. To avoid the influence of dominant personalities and overrepresentation of the individual opinions or views of experts, the guideline team reached consensus when the evidence base was inconsistent, weak, or lacking. The matrix in Table 3 (see the original guideline) assisted in the assignment of final grades to recommendations. The methodology expert pregraded recommendations by using the information in columns 5, 6, and 7 of the evidence tables provided by committee members (see Table 3 in the Appendix to the original guideline). Authors reviewed these grades and returned the amended evidence tables to the methodology expert for completion. Committee members added comments or explanatory notes when necessary (column 8) to enhance the transparency and reproducibility of the considered judgment and consensus process of grading and to address the adaptability and applicability of the final recommendations. All sections were reviewed by the American Diabetic Association (ADA) representative, a clinical expert, and a methodology expert and were edited by the chairman of the guideline committee.

Rating Scheme for the Strength of the Recommendations

Grading the Strength of Recommendations

A. The National Academy of Clinical Biochemistry (NACB) Strongly Recommends Adoption.

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- There is moderate-quality evidence and strong or very strong agreement of experts that the intervention improves important health outcomes and that benefits substantially outweigh harms.

Strong recommendations *against* adoption are made when:

- There is high-quality evidence and strong or very strong agreement of experts that the intervention is ineffective or that benefits are closely balanced with harms, or that harms clearly outweigh benefits; *or*
- There is moderate-quality evidence and strong or very strong agreement of experts that the intervention is ineffective or that benefits are

closely balanced with harms, or that harms outweigh benefits.

B. The NACB Recommends Adoption.

Recommendations *for* adoption are made when:

- There is moderate-quality evidence and level of agreement of experts that the intervention improves important health outcomes and that benefits outweigh harms; *or*
- There is low-quality evidence but strong or very strong agreement and high level of confidence of experts that the intervention improves important health outcomes and that benefits outweigh harms; *or*
- There is very low-quality evidence but very strong agreement and very high level of confidence of experts that the intervention improves important health outcomes and that benefits outweigh harms.

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- There is moderate-quality evidence and level of agreement of experts that the intervention is ineffective or that benefits are closely balanced with harms, or that harms outweigh benefits; *or*
- There is low-quality evidence but strong or very strong agreement and high level of confidence of experts that the intervention is ineffective or that benefits are closely balanced with harms, or that harms outweigh benefits; *or*
- There is very low-quality evidence but very strong agreement and very high level of confidence of experts that the intervention is ineffective or that benefits are closely balanced with harms, or that harms outweigh benefits.

C. The NACB Concludes That There Is Insufficient Information to Make a Recommendation.

Grade C is applied in the following circumstances:

- Evidence is lacking, scarce, or of very low quality, the balance of benefits and harms cannot be determined, and there is no or very low level of agreement of experts for or against adoption of the recommendation.
- At any level of evidence—particularly if the evidence is heterogeneous or inconsistent, indirect, or inconclusive—if there is no agreement of experts for or against adoption of the recommendation.

Good Practice Point (GPP). The NACB Recommends It as Good Practice Point.

GPPs are recommendations mostly driven by expert consensus and professional agreement and are based on the information listed below and/or professional experience, or widely accepted standards of best practice. This category applies predominantly to technical (e.g., preanalytical, analytical, postanalytical), organizational, economic, or quality management aspects of laboratory practice. In these cases, evidence often comes from observational studies, audit reports, case series or case studies, nonsystematic reviews, guidance or technical documents, non–evidence-based guidelines, personal opinions, expert consensus, or position statements. Recommendations are often based on empirical data, usual practice, quality requirements, and standards set by professional or legislative authorities or accreditation bodies, etc.

Cost Analysis

- The cost-effectiveness of screening for type 2 diabetes has been estimated. The incremental cost of screening all persons ≥25 years has been estimated to be $236,449 per life-year gained and $56,649 per quality adjusted life-year (QALY) gained. Interestingly, screening was more cost-effective at ages younger than the 45 years currently recommended. In contrast, screening targeted to individuals with hypertension reduces the QALY from $360,966 to $34,375, with ages between 55 and 75 years being the most cost-effective.
- A cost-effectiveness analysis of data from the Diabetes Glycaemic Education and Monitoring (DiGEM) trial concluded, "Self monitoring of blood glucose with or without additional training in incorporating the results into self care was associated with higher costs and lower quality of life in patients with non-insulin treated type 2 diabetes. In light of this, and no clinically significant differences in other outcomes, self monitoring of blood glucose is unlikely to be cost effective in addition to standardised usual care".
- Published studies have demonstrated that it is cost-effective to screen all patients with diabetes and/or kidney disease for albuminuria.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The second draft of the guideline with graded recommendations was posted on the National Academy of Clinical Biochemistry (NACB) Web site for a last call for public comments. The guideline recommendations were also reviewed by the Professional Practice Committee of the American Diabetic Association (ADA). Several comments were received and incorporated, and the final guideline draft was submitted for review by the joint Evidence-Based Laboratory Medicine Committee of the American Association for Clinical Chemistry (AACC) and the NACB. After addressing the reviewers' comments, the guideline committee referred the guideline to the NACB Board of Directors, which approved it before its official release for publication. This guideline was approved by the NACB Board of Directors in January 2011.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate laboratory analysis in the diagnosis and management of diabetes mellitus

Potential Harms

Not stated

Qualifying Statements

Qualifying Statements

During the considered-judgment process, the guideline committee was primarily driven by two core bioethical values—beneficence and nonmalevolence. The guideline group also observed the first principle of bioethics (i.e., respect for patients' autonomy and the decision-making capacities of individuals to make their own choices). The guideline group assumes that the target users will also deal with this core bioethical principle when using these guidelines in practice. The guideline committee acknowledges that it was not able to cover universally other bioethical principles, such as justice and equity. The members of the guideline team, as well as individuals who commented on the recommendations, were mostly from North America and other developed countries. Their views and experiences therefore unavoidably affected the considered-judgment and consensus processes involved in formulating recommendations. The guideline team also could not consider explicitly the cost implications of the recommendations in various resource settings, although recommendations were formulated in a generic way and in a cost-conscious manner.

Implementation of the Guideline

Description of Implementation Strategy

To assist implementation, key recommendations of the guideline and their grades are summarized in the original guideline. Key diagnostic and risk assessment criteria are presented in tables, and a diagnostic algorithm is provided for urinary albumin testing (see the original guideline). Most recommendations are worded to represent standards of care and thus can be easily converted to key performance indicators for local audit purposes.

Although recommendations have been developed for national and international use and are intended to be generic, certain elements of this guideline will not reflect views that are universally held, and other elements may have limited applicability in healthcare settings that lack sufficient resources for adopting the recommendations. The guideline committee advises users to adapt recommendations to their local settings. During such adaptation processes, the evidence tables provided (see Table 3 in the Appendix to the original guideline) might assist users in making informed decisions.

Implementation Tools

Clinical Algorithm

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Academy of Clinical Biochemistry (NACB). Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. Washington (DC): National Academy of Clinical Biochemistry (NACB); 2011. 104 p. [378 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2002 (revised 2011)

Guideline Developer(s)

National Academy of Clinical Biochemistry - Professional Association

Source(s) of Funding

National Academy of Clinical Biochemistry

Guideline Committee

National Academy of Clinical Biochemistry Committee

Composition of Group That Authored the Guideline

Primary Authors: David B. Sacks, Department of Laboratory Medicine, National Institutes of Health, Bethesda, MD; Mark Arnold, Department of Chemistry, University of Iowa, Iowa City, IA; George L. Bakris, Department of Medicine, Hypertensive Disease Unit, Section of Endocrinology, Diabetes and Metabolism, University of Chicago, Chicago, IL; David E. Bruns, Department of Pathology, University of Virginia Medical School, Charlottesville, VA; Andrea Rita Horvath, Screening and Test Evaluation Program, School of Public Health, University of Sydney, SEALS Department of Clinical Chemistry, Prince of Wales Hospital, Sydney, Australia; M. Sue Kirkman, American Diabetes Association, Alexandria, VA; Ake Lernmark, Department of Clinical Sciences, Lund University/CRC, Skane University Hospital Malmö, Malmö, Sweden; Boyd E. Metzger, Division of Endocrinology, Northwestern University, Feinberg School of Medicine, Chicago, IL; David M. Nathan, Massachusetts General Hospital and Harvard Medical School, Diabetes Center, Boston, MA, and Pathobiology, University of Toronto, Ontario, Canada

Financial Disclosures/Conflicts of Interest

All authors who contributed to the development of the recommendations of this guideline have declared (via the official disclosure form of the National Academy of Clinical Biochemistry [NACB]) any financial, personal, or professional relationships that might constitute conflicts of interest with this guideline. These disclosures are part of the guideline document published on the NACB Web site .

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Employment or Leadership: D.B. Sacks, *Clinical Chemistry*, American Association of Clinical Chemistry (AACC); M. Arnold, ASL Analytical, Inc.; G.L. Bakris, American Society of Hypertension and National Kidney Foundation; D.E. Bruns, *Clinical Chemistry*, AACC.

Consultant or Advisory Role: G.L. Bakris, Novartis, Merck, Walgreen Co., and Takeda; A. Lernmark, Diamyd Medical AB and Probi AB.

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Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Sacks DB, Bruns DE, Goldstein DE, Maclaren NK, McDonald JM, Parrott M. Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. Clin Chem 2002 Mar;48(3):436-72.

The next review of this guideline is planned in 5 years, unless substantial new evidence emerges earlier for high-priority areas in the laboratory management of patients with diabetes mellitus.

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the National Academy of Clinical Biochemistry (NACB) Web site .

Print copies: National Academy of Clinical Biochemistry publications are available through American Association for Clinical Chemistry (AACC) Press. To make a purchase or request a catalog, contact AACC Customer Service at 202-857-0717 or custserv@aacc.org.

Availability of Companion Documents

None available

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI on April 10, 2003. The information was verified by the guideline developer on June 5, 2003. This NGC summary was updated by ECRI Institute on October 6, 2011. The information was verified by the guideline developer on November 3, 2011.

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